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Case Report

A Case Of Nephrotic Syndrome In A Context Of Sexual Ambiguity.

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Abstract

We report a case of a 07-year-old child admitted to the pediatric emergency department of CHU Gabriel Touré for oedemato-ascitic syndrome. At admission, constants were as follows: temperature 37°C, heart rate 122/min, respiratory rate 40/min, blood pressure 130/90 mmHg. The child weighed 23 kg and measured 120 cm. His head circumference was 42 cm. There was mild pallor, facial swelling and oedema of the lower limbs. Pseudoscrotal fused genital bulges were present, without the testicles inside. The urethral meatus at the level of the glans was absent. The hypospadias was scrotal. Sexual ambiguity corresponded to Prader stage 5. Urine dipstick showed four-cross proteinuria. Proteinuria of 104 mg/kg/24h (2.4g/kg/24h) led to the diagnosis of nephrotic syndrome. The blood albumin level had dropped to 26g/l, with haematological (Hb: 8g/dl) and renal (creatinine 850 µmol/l, i.e. 16XN; urea 40 mmol/l) findings. ATL - SRY gene testing by PCR-multiplex on whole blood revealed XY in favour of male sex. The onset of nephrotic syndrome in a sexually ambiguous setting prompted us to consider Denys-Drash syndrome. The patient received four sessions of hemodialysis. Prednisone-based corticosteroid therapy (60mg/m2/d) was initiated. On day 2 of treatment, the urine strip showed proteinuria at four points. On the third day of corticosteroid therapy, the patient developed malignant hypertension (BP= 16/11 mm Hg), anuria and moderate epistaxis. He died two hours later.

Conclusion: A nephrotic syndrome occurring in a sexually ambiguous presentation should suggest Denys-Drash syndrome. The prognosis of this genetic disorder is poor.

Keywords: nephrotic syndrome, sexual ambiguity, Denys-Drash syndrome

INTRODUCTION

The occurrence of nephrotic syndrome in the context of sexual ambiguity is rare. About 150 cases have been described in the literature. Glomerular nephropathy associated with genital anomalies leads clinicians to investigate Denys Drash syndrome [1,2]. Denys Drash syndrome is an autosomal dominant genetic disorder linked to a mutation in the WT1 gene, located on chromosome 11. This gene codes for the WT1 protein, which plays a regulatory role in the development of the kidneys and genital organs during pregnancy. The management of glomerular kidney disease is a challenge, given the acute, life-threatening complications. We report a case diagnosed and managed in the pediatric department of CHU Gabriel Touré.

CASE REPORT

This case concerns the child A.K, aged 07 years, referred to the pediatric emergency department of Gabriel Touré University Hospital for oedemato-ascitic syndrome. He had been reportedly suffering from this condition for a month, marked by the onset of hypogastric pain of 3/10 intensity. The pain was intermittent, not radiating, and was relieved using paracetamol. Facial swelling and abdominal tenderness were noted one week later. An abdominal ultrasound performed at the local hospital revealed moderate amounts of ascites. Both kidneys were normal. The child was born of a full-term pregnancy. Ante-natal ultrasound examinations performed in the second and third trimesters were unremarkable, and failed to determine the sex of the fetus. At birth, the fetus weighed 3kg, measured 50 cm in height and had a head circumference of 35cm. A detailed somatic examination during the first week of life was not performed. He is attending school and performing well. According to the national vaccination program, the child was well vaccinated. He had a history of recurrent angina. Hematuria was absent. He is the fifth child in his sibling group. All siblings were in good health. On admission, vitals were as follows: temperature 37°C, HR 122/min, FR 40/min, P.A 130/90 mmHg. The child weighed 23 kg and was 120 cm tall. His head circumference was 42 cm. The skin was moderately pale, the face puffy and the lower

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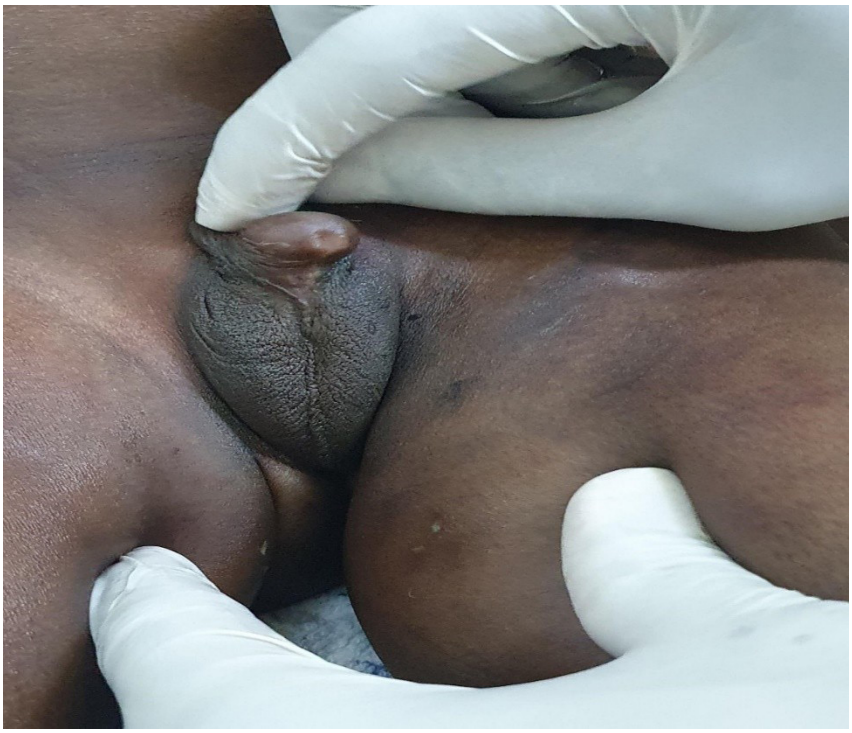
limbs oedematous. Palpation of the liver, spleen and lymph nodes were all normal. Pseudoscrotal fused genital bulges were present, without the testicles inside. The urethral meatus at the level of the glans was absent. The hypospadias was scrotal. Sexual ambiguity corresponded to Prader stage 5 (**Fig.1**). The urine dipstick showed four-cross proteinuria. The rest of the physical examination was unremarkable.

Figure 1. patient's external genital organs



The diagnosis of nephrotic syndrome was confirmed on the basis of proteinuria at 104 mg/kg/24h (2.4g/kg/24h). The albumin level had dropped to 26g/l, with haematological (Hb: 8g/dl) and renal (creatinine 850 µmol/l, i.e. 16XN; urea 40 mmol/l) complications. The report of the second abdominal ultrasound was as follows: Adrenal glands not visible, presence of female-type internal genital organs with presence of right ovary; left ovary not visualized; testicles not visualized intra-abdominally. ATL - SRY gene testing by PCR-multiplex on whole blood gave XY in favour of male sex. The WT1 gene was not tested for mutation. Given the occurrence of nephrotic syndrome in a sexually ambiguous setting, we considered Denys-Drash syndrome. The patient received four sessions of hemodialysis. Prednisone-based corticosteroid therapy (60mg/m2/d) was initiated. On day 2 of treatment, the urine dipstick showed proteinuria at four crosses. On the third day of corticosteroid therapy, the patient developed malignant hypertension (BP= 16/11 mm Hg), anuria and moderate epistaxis. Unfortunately, he died two hours later.

DISCUSSION

Our patient was diagnosed with nephrotic syndrome at the age of 7. The main feature of his nephropathy was hydrops. The diagnosis could not be established antenatally or during the neonatal period. The presence of clinical sexual ambiguity requires long-term monitoring. Glomerular damage can be detected early by testing for proteinuria using dipsticks. The combination of proteinuria and sexual ambiguity suggests two main syndromes: Denys-Drash syndrome and Frasier syndrome [3,4,5]. Both syndromes are expressed by the association of sexual ambiguity (phenotypic or genotypic) and a nephrotic syndrome [6]. Distinguishing between the conditions is not always easy, due to their highly variable clinical expressions. The existence of distinctive epidemiological, clinical, anatomical-pathological, biological and evolutionary criteria makes it possible to distinguish between the two syndromes. Epidemiologically, Frasier syndrome is most often found in subjects with a female phenotype, whereas Denys Drash syndrome is defined by male pseudohermaphroditism [7]. Denys Drash syndrome is an autosomal dominant genetic disorder caused by a mutation in the WT1 gene, located on chromosome 11 [8]. This gene codes for the WT1 protein, which plays a regulatory role in the development of the kidneys and genital organs during pregnancy. A defect in this protein leads to glomerular structural anomalies and abnormalities in sexual development. This is a syndrome predisposing to nephroblastoma. It occurs when the child has a mutated gene, which may be inherited from a parent or appear de novo in the child. Nephrotic syndrome in Denys Drash syndrome is

expressed very early in the child's life, most often before the 3rd month of life [9]. Cortico-resistance and complications are frequent. In our patient, renal biopsy was not performed, but does not make a significant diagnostic contribution in cases of corticoresistance. The most common pathological lesion in Denys Drash syndrome is diffuse mesangial sclerosis, which presages a severe nephrotic syndrome with corticoresistance [10,11].From a biological point of view, ATL - SRY gene testing by PCR-multiplex on whole blood gave XY in favor of male sex. The WT1 gene was not tested for mutation. Our patient had massive proteinuria (104 mg/kg/24 hours), and his albumin level had collapsed (to 26g/l). The impact was hematological (Hb: 8 g/dl) and renal (creatinine 850 µmol/l, i.e. 16XN; urea 40 mmol/l). In Denys Drash syndrome, progression to renal failure occurs earlier (between 1 and 3 years) than in Frasier syndrome, where it occurs in adolescence [12]. The same applies to the occurrence of nephroblastoma. On admission, renal function was impaired and no signs of nephroblastoma were detected. Management of Denys Drash syndrome begins with treatment of the nephropathy, which will ensure the child's survival until kidney transplantation. Renal damage is very severe, and exposes the patient to infectious, thromboembolic and nutritional complications, which can rapidly become life-threatening. The management of these complications requires an adequate technical support facility, which is the reason for the high mortality of patients at the initiation of corticosteroid therapy in developing countries [13]. Further treatment requires hemodialysis and early transplantation. Our patient received four sessions of hemodialysis coupled with the start of prednisone-based corticosteroid therapy (60mg/m2/d). On day 2 of treatment, the urine dipstick showed proteinuria at four crosses. On the third day of corticosteroid therapy, the patient developed malignant hypertension (BP= 16/11 mm Hg), anuria and moderate epistaxis. Unfortunately, he died two hours later.

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